09/916214

Express Mail Label No. EV 336 039 871 US Attorney Docket No. 37167-8040.US00

Amendments to the Specification

insert this before the heading Field ... Bd 6/9/08

On page 1, please ~~replace the~~ paragraph ~~starting on line 7~~ with the following:

This application claims the benefit of priority to US Provisional Application Serial No. 60/220,639, filed July 25, 2000, entitled "Tissue, Monitoring and Characterization Apparatus and Method", which is fully incorporated by reference herein. This application is also related to co-pending ~~application attorney docket number 13724-850~~US Patent Application No. 09/916,235, filed July 25, 2001, which is also fully incorporated by reference herein.

On page 6, please replace the paragraph starting on line 4 with the following:

Figures 4a-4[[c]]d are perspective views illustrating various arrangements of the emitting and detecting members; Figures 4a-4b illustrate[[s]] an embodiment having a centrally positioned a return electrode surrounded by other impedance sensing members; Figure 4[[b]]c illustrates an embodiment having the return electrode eccentrically positioned respect to other impedance sensing members; Figure 4[[c]]d illustrates an embodiment having multiple and independently positionable impedance sensor arrays.

On page 13, please replace the paragraph starting on line 19 with the following:

Referring now to Figures 1 and 2, an embodiment of impedance treatment apparatus 10 comprises an elongated member or introducer 12 having a lumen 13, a proximal portion 14, a distal end 16, one or more resilient members 18 positionable in lumens 13 and one or more impedance sensors 22 disposed on members 18 or impedance sensing members 22m positionable in lumens 72 disposed within members 18. Distal end 16 may be sufficiently sharp to penetrate tissue including fibrous and/or encapsulated tumor masses, bone, cartilage and muscle. Lumens 13 may extend over all or a portion of the length of introducer 12. Members 18 can comprise a plurality 18pl of resilient members 18 configured to be positionable in lumen 13 and advanceable in and out of distal end 16 by an advancement device 15 or advancement member 34 or other means described herein. Resilient members 18 can be deployed with curvature

09/916214 B)

Express Mail Label No. **EV 337 198 772 US** Attorney Docket No. 37167-8040.US00 (13724-849)

Amendments to the Specification

PG 6/9/08

On page 1, please replace the paragraph starting on line ~~15~~ 6 with the following:

This invention relates generally to a method for performing tissue characterization using minimally invasive methods. More particularly, the invention relates to a method and apparatus for performing an in vivo tissue characterization to identify and discriminate between diseased and healthy tissue using localized measurement of tissue impedance. Still more particularly, the invention to relates to a method and apparatus for performing tissue characterization before during and after ablative therapy using localized complex impedance measurement to monitor and titrate the delivery of ablative therapy to improve clinical outcomes.

On page 2, please replace the paragraph starting on line 30 with the following:

The apparatus can be configured to detect, locate and identify tumorous tissue at a selected tissue site using impedance measurements such as multi-pathway measured impedance, complex impedance and impedance vector measurements. For complex impedance real and imaginary components of the impedance signal can be used to determine more refined bioelectric parameters such as interstitial and intracellular impedance and cell membrane capacitance that provide greater sensitivity and predictive power of cell necrosis or malignancy. Also, the apparatus can ~~also~~ be configured to utilize one or more impedance measurements to monitor a target tissue site and control the course of ablative therapy before during or after the delivery of ablative energy or other treatment to the tissue site. Accordingly the apparatus can be configured to be used independently or in conjunction with another ablative apparatus such as an RF, microwave or laser ablation apparatus. Further, the apparatus can be configured to utilize multi-path impedance measurement to monitor two or more tissue volumes including a tumor volume, a developing ablation volume and an adjacent anatomical structure. Additional embodiments of the apparatus can also be configured to utilize impedance measurements such as complex, vector or locus impedance measurements to generate an image of a target tissue site and display the image to facilitate the location and monitoring of a tumor and/or ablation volume.

presented on the background of tissue monitoring and identification using impedance measurement. Owing to variations in composition and morphology various tissue types have different electrical properties (*e.g.* conductance, inductance, capacitance *etc.*) and therefore conduct electrical energy differently particularly at certain frequencies. For example, cancerous tissue will typically have a significantly higher phase than the health tissue, particularly at low frequencies. These differences in electrical properties, particular conductance result, in a characteristic impedance profile 19p for a given tissue type or condition when the tissue is exposed to an excitation current at one or more specific frequencies. Impedance profile 19p can have one or more peaks 19pk, curves and other shapes that serve as a fingerprint of the tissue type or tissue condition. Accordingly by analyzing the impedance profile 19p and matching peaks, curve shapes, thresholds etc, profile 19p can be utilized by embodiments of the invention to identify tissue types and conditions such as malignancy, vascularity, necrosis, thermal injury *etc.* Related conditions that can also be identified using this approach include abnormally mutated tissue, abnormally dividing tissue or hypoxic tissue.

On page ~~29~~ 30, please replace the paragraph starting on line 24 with the following: PP 6/9/08

As described herein, in various embodiments all or a portion of resilient member 18 can be an energy delivery device or member 18e. Turning to a discussion of energy delivery device and power sources, the specific energy delivery devices 18e and power sources 20 that can be employed in one or more embodiments of the invention include but are not limited to, the following: (i) a microwave power source coupled to a microwave antenna providing microwave energy in the frequency range from about 915 MHz to about 2.45 GHz (ii) a radio-frequency (RF) power source coupled to an RF electrode, (iii) a coherent light source coupled to an optical fiber or light pipe, (iv) an incoherent light source coupled to an optical fiber, (v) a heated fluid coupled to a catheter with a closed or at least partially open lumen configured to receive the heated fluid, (vi) a cooled fluid coupled to a catheter with a closed or at least partially open lumen configured to receive the cooled fluid (viii) a cryogenic fluid, (ix) a resistive heating source coupled to a conductive wire, (x) an ultrasound power source coupled to an ultrasound emitter, wherein the ultrasound power

09/916 214
B1

source produces ultrasound energy in the range of about 300 KHZ to about 3 GHz, (xi) and combinations thereof. For ease of discussion for the remainder of this application, the energy delivery device 18e is one or more RF electrodes 18e and the power source utilized is an RF power supply. For these and related embodiments, RF power 20 supply can be configured to deliver 5 to 200 watts, preferably 5 to 100, and still more preferably 5 to 50 watts of electromagnetic energy ~~is~~ to the electrodes of energy delivery device 18 without impeding out. The electrodes 18e are electro magnetically coupled to energy source 20. The coupling can be direct from energy source 20 to each electrode 18e respectively, or indirect by using a collet, sleeve and the like which couples one or more electrodes to energy source 20.

On page ~~30~~ 31, please replace the paragraph starting on line 19 with the following:

P.N. 6/9/08

In various embodiments, electrodes 18e ~~including~~include impedance sensors 22 and sensing members 22m can have a variety of shapes and geometries. Referring now to Figures 15a-15f, example shapes and geometries can include, but are not limited to, ring-like, ball, hemispherical, cylindrical, conical, needle-like and combinations thereof. Referring to Figure 16, in an embodiment electrode 18e can be a needle with sufficient sharpness to penetrate tissue including fibrous tissue including, encapsulated tumors cartilage and bone. The distal end 18de of electrode 18e can have a cut angle 68 that ranges from 1 to 60°, with preferred ranges of at least 25° or, at least 30° and specific embodiment of 25° and 30°. The surface of electrode 18e can be smooth or textured and concave or convex. Electrode 18e can have different lengths 38 that are advanced from distal end 16' of introducer 12. The lengths can be determined by the actual physical length of electrode(s) 18e, the length 38' of an energy delivery surface 18eds of electrode 18e and the length, 38" of electrode 18e that is covered by an insulator 36. Suitable lengths 38 include but are not limited to a range from 1-30 cms with specific embodiments of 0.5, 1, 3, 5, 10, 15 and 25.0 cm. The conductive surface area 18eds of electrode 18e can range from 0.05 mm2 to 100 cm2. The actual lengths of electrode 18e depend on the location of tissue site 5' to be ablated, its distance from the site, its accessibility as well as